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EDITORIAL COMMENT

Left Atrial Function in Mitral Regurgitation

Guilt by Association*

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Despite decades of study and literally hundreds of papers in the medical literature, the management of patients with mitral regurgitation (MR) caused by myxomatous mitral valve disease remains the subject of ongoing uncertainty and controversy (1–3). Current indications for surgical intervention that rely on symptoms, left ventricular (LV) systolic function, atrial fibrillation, and pulmonary artery pressure, which are embedded in the American and European practice guidelines (4,5), are based on evidence that these subjective and objective markers

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of disease severity have a demonstrable impact on patient outcomes. It is also understood that when significant symptoms, LV dysfunction, atrial fibrillation, and/or pulmonary hypertension develop in patients, their survival and functional results after mitral valve repair are suboptimal compared with patients who undergo surgery earlier in the natural history of the disease (1,3,6–9). This has resulted in a trend toward earlier referral for surgery in patients with severe MR, even if they are asymptomatic with preserved systolic function, when there is a high likelihood of successful and durable mitral valve repair (4). It is further recognized that additional objective markers indicative of outcome would help greatly in refining this complex clinical decision-making process.

For such a new marker to fulfill this need, it must be shown to be independent of the existing markers and provide incremental information regarding patient outcomes above and beyond that provided by the existing markers. That is, it must be useful in identifying patients who will benefit from early surgery who are not already so identified based on the established indications for surgery. This is not an issue for managing mitral valve disease alone but is true in diagnostic testing in all areas of cardiovascular medicine, in which novel risk markers should have calibration (correctly identifying the proportion of patients who will have an event) and discrimination (distinguishing between patients at higher and lower risk) and thus reclassify patients according to risk (10). Examples of this effect include C-reactive protein and coronary calcium scoring in reclassifying the risk of coronary heart disease events beyond the Framingham risk score (11,12). The study by Ring et al. (13) in this issue of *iJACC*, proposing that measures of left atrial function can serve as a guide to optimal timing of surgery for myxomatous MR, fails to achieve this standard. This study reports associations between left atrial function and the conventional indications for surgery, but does not show incremental diagnostic or prognostic value, and it provides no outcome data.

For several years, the response of the left atrium to chronic severe MR has been a focus of investigation (14,15), moving beyond the more customary assessments of LV volume and function, quantification of MR severity, and pulmonary artery pressure. The magnitude of left atrial dilation has been shown to be a determinant of outcome in patients with severe MR that is additive to the standard indications for surgery (16,17). As a result, severe left atrial dilation on echocardiography (>60 ml/m^2) appeared as a new Class IIb recommendation for consideration for surgical mitral valve repair in the

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2012 guidelines of the European Society of Cardiology (5).

In the current paper, Ring et al. (13) further explore the left atrial response to chronic myxomatous MR by assessing left atrial contractile function in patients with mild to moderate MR, asymptomatic patients with severe MR without standard indications for surgery, and patients with severe MR who fulfilled criteria for surgery. Using 2-dimensional echocardiography and 2-dimensional speckle tracking, they report that left atrial ejection fraction and left atrial strain patterns are "independent predictors" of indications for surgery and conclude that assessment of left atrial function by echocardiography is an additional tool to guide the optimal timing of surgery for myxomatous MR.

Ring et al. (13) have shown interesting and noteworthy associations between left atrial function and the currently accepted consensus-driven indicators for surgery. However, these are associations only, and they have not shown that the measures of left atrial function are predictive of outcome or that they provide incremental diagnostic or prognostic potential to guide management. The terms *predict* and *independent* are used very loosely in a cross-sectional study with no follow-up information. The patients who fulfilled standard criteria for surgery were older and more symptomatic and had worse LV function (mean end-systolic dimension of 50 mm), higher pulmonary artery systolic pressures, and markedly greater left atrial volumes (mean 71 ml/m^2). Thus, it should come as no surprise that other measures of disease severity, such as left atrial contractile function, were more abnormal in this group. One does not need some new index to recognize these patients as being sicker and needing surgery. But how well do the left atrial function data behave in the asymptomatic group who do not already have indications for surgery in actually predicting who will either develop indications for surgery in the future or have a worse outcome?

Thus, the current paper provides the basis for future work to explore the potential of left atrial functional assessment in guiding management decisions. However, it is an overly zealous interpretation of the current state of knowledge to suggest that these measurements represent a new predictive instrument when there has been no attempt to tie them to outcomes. Unfortunately, the authors use the term *predict* in its various iterations 14 times, and *independent* is repeated 11 times. The association with the other established predictors of poor outcome is not evidence of an independent new predictor because, by definition, the new variables are dependent on the existing predictors. The demonstration that patients who are older, sicker (more symptomatic), and with worse LV function and higher pulmonary artery pressures also have worse left atrial function does not lead to the conclusion that assessment of left atrial function is an independent predictor of the need for surgery. What is now needed is further application of these novel measurements to a younger, less sick population being followed serially to determine whether they indeed predict the need for surgery above and beyond the customary variables. Also, do these measurements predict poor outcome after surgery in some manner not predicted by age, symptoms, LV size and function, and pulmonary artery pressure? This challenge should be the basis for future studies to determine whether these indexes actually do provide independent, incremental value in patient management.

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Key Words: atrial function ■ mitral valve prolapse ■ mitral valve surgery.